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When is "aristolochic acid nephropathy" more accurate than "Chinese herbs nephropathy"?

To the Editor: In their letter entitled "Time to abandon the term 'Chinese herbs nephropathy'" in the November issue of *Kidney International*, Dr. Chen et al argue against continuing to use the term "Chinese herbs nephropathy" to describe the rapidly progressive sclerosing interstitial nephropathy observed in women given Chinese herbs for slimming purposes [1].

In a recent case report published in the electronic Website edition of the November issue of *American Journal of Kidney Disease*, we demonstrated that aristolochic acid (AA) taken in China in an herbal remedy induces a typical Chinese herbs nephropathy (CHN) with AA-DNA adducts and urothelial lesions [2]. Furthermore, AA given alone to rabbits induces similar renal and urothelial lesions [3]. The causal role of AA in the Belgian epidemy and in at least one Chinese patient is thus established. We have proposed to use the term "aristolochic acid nephropathy" in those cases in which there is unequivocal demonstration of AA intoxication.

Second, in a Letter to the Editor in the same issue of *American Journal of Kidney Disease*, Solez et al commented on Dr. Chen's original posting and subsequent discussion on the AJKD Discussion Forum and on the NEPHROL E-mail discussion group. He argued that self-regulation was preferable to editorial decisions [4]. He emphasized the difficulty to determine the content of herbal preparations. The term CHN had never intended to denigrate the system of Chinese herbal medicine. Indeed, many useful compounds widely used in Western medicine came from Chinese herbal medicine.

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Bone alkaline phosphatase isoforms in chronic renal failure

To the Editor: Congratulations to Magnusson et al for their article about bone-specific alkaline phosphatase (bAP) and its isoforms [1]. They identified a new serum bAP isoform (B1x) in ESRD patients. However, several points need clarification. First, why did end-stage renal disease (ESRD) patients have elevated total AP activity? Did any of the patients have any hepatic disorder such as hepatitis B or C? If not, then an increase in B2 bAP isoform, produced by trabecular osteoblasts, will take an enormous clinical value. Second, since B2 represents more than 35% of the total bAP activity and B1 only 4%, could the 5-fold increase of B2 solely explain the 2.6-fold increase in total AP activity? Third, was there any difference in the absolute values of bAP [2], both mass and activity, between healthy subjects and ESRD patients? Fourth, we and other authors have shown that bAP positively correlate with PTH [3, 4]. How do Magnusson et al explain the absence of such a correlation in their present study?

Finally, without bone histology, the suggestion that B1x is a marker of adynamic bone is hazardous. Certainly, patients with positive B1x had several elements in favor of adynamic bone, including old age, low bAP, and osteocalcin. However, the same patients had parathyroid hormone (PTH) levels 2 to 10 times greater than the normal values, and serum CrossLaps significantly increased. This suggests either increased bone resorption or uncoupling between bone formation and bone resorption rates. Were these patients osteopenic or osteoporotic on bone mineral density?

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Reply from the authors

We welcome the letter from Dr. Ureña Torres as it offers us an opportunity to clarify and emphasize several aspects of our measurements of the different bone alkaline phosphatase (BALP) isoforms in patients with chronic renal failure (CRF) [1]. In reply to his queries regarding questions 1 and 2, total ALP was significantly increased; however, the majority of the patients had activities within the reference interval for healthy adults. We agree with the suggestion that the increase of BALP isoform B2 in CRF patients may be clinically useful. None of the patients in this study had any biochemical or clinical evidence of hepatic disorder. To answer the third question, we used the previously reported reference intervals for all three BALP immunoassay kits (Alkphase-B, Tandem-R Ostase and Tandem-MP Ostase) and refer him to Figure 2 [1]. To respond to his fourth question, discordant findings between different studies are not uncommon, which probably reflects the heterogeneity of bone disorders in CRF patients. We did, however, find a significant correlation between the novel BALP isoform B1x and PTH, which might contribute to the positive correlations previously reported [2].

We suggested that B1x should be further evaluated as a marker of adynamic bone disease. This will indeed require a classification of patients by bone histomorphometry, which was not obtained in this study. Although adynamic bone disease is usually associated with relatively low parathyroid hormone (PTH) levels, PTH may fail to discriminate between adynamic and moderate hyperparathyroid states and even high PTH levels may occur [3]. Another important point, discussed in our paper [1], is that PTH was analyzed using a commercial assay originally reported to detect only the intact (1-84 PTH) circulating molecule. However, it has recently been demonstrated that a fragment (most likely the 7-84 PTH) interferes with this assay [4]. Thus, the PTH values reported in our study (and other studies) might well be higher than the true circulating levels of intact 1-84 PTH. Bone mineral density was not assessed and we prefer not to speculate as to whether these patients were osteopenic or osteoporotic.

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Prediction of hypertension in hemodialysis patients

To the Editor: I have read with much interest the paper by Agarwal and Lewis [1] on prediction of hypertension in chronic hemodialysis patients. In the introduction, the authors focus on the fact that it is still uncertain which blood pressure measurement the clinician has to adopt to define hypertension in these patients. There is no question that in the general population 24-hour ambulatory monitoring is a better measure than the office measure. It is well-documented that the ambulatory estimate is superior to the office estimate for predicting incident cardiovascular complications, as well as left ventrical hypertrophy (LVH) [2], which is a valid surrogate end point. Whether or not 24-hour ambulatory monitoring predicts survival and cardiovascular complications in the dialysis population still remains to be proved. This is important mostly because two surveys have shown that routine pre-dialysis blood pressure and 24-hour ambulatory monitoring explain to a similar degree the variance in left ventricular mass. Both the paper by Conlon et al [3] and our study based on multivariate modelling [4] have clearly shown the strength of the association between 24-hour ambulatory monitoring and left ventrical mass is not superior to that of pre-dialysis blood